Propagation, rethrombosis and new thrombus formation after acute deep venous thrombosis

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Purpose: **The purpose of this study was to determine the incidence, timing, and outcome of further thrombotic events after an initial episode of acute deep venous thrombosis.**
Methods: **Venous thrombi in 204 lower extremities (177 patients) were monitored with duplex ultrasonography at intervals of 1 day, 7 days, 1 month, every 3 months for 1 year, and yearly thereafter.**
Results: **Among initially involved extremities, propagation to new segments occurred in 61 (30%) and rethrombosis occurred in 63 (31%). Both propagation and rethrombosis, in different segments, occurred in 27 (13%) extremities. New thrombi were also noted in nine (6%) initially uninvolved extremities. These events were not associated with identifiable clinical risk factors, although extremities with rethrombosis were more extensively involved at presentation. Propagation in initially involved extremities was an early event, occurring within a median of 40 days in all segments. New thrombotic events in initially uninvolved extremities and rethrombosis occurred as later events. The development of reflux was significantly more common among all initially uninvolved segments to which thrombus extended and among mid and distal superficial femoral and popliteal artery segments with rethrombosis.**
Conclusions: **Recurrent thrombotic events are common after acute deep venous thrombosis and adversely affect the ultimate development of valvular incompetence. Their occurrence is unrelated to recognized clinical risk factors and can occur despite standard anticoagulation measures. (J VASC SURG 1995;22:558-67.)**

Recanalization of the venous lumen is now recognized as a common phenomenon after an episode of deep venous thrombosis (DVT).[1-4] However, further thrombotic events, including extension of thrombus to previously uninvolved segments and rethrombosis of involved segments, have also been recognized clinically and in natural history studies of acute DVT. Indeed, thrombus evolution is perhaps best regarded as a dynamic process, with recanalization and further thrombotic events occurring as competing processes in many patients. The balance between these processes seems to favor recanalization in most patients, resulting in eventual reestablishment of the venous lumen. However, thrombotic events occurring after initial presentation may have important implications for valve function and eventual development of the postthrombotic syndrome. Furthermore, both propagation[5] and rethrombosis[6] have been associated with an increased risk of pulmonary embolism.

The determinants of valve function after an acute DVT remain incompletely understood. The time required for complete recanalization has previously been shown to be an important determinant of valve competence.[2] However, lysis times are not the sole determinant of valve function as illustrated by the small number of venous segments eventually developing reflux despite relatively rapid lysis. It is likely that other factors, including further thrombotic insults, contribute to the eventual development of reflux.

The purpose of this study was to determine the incidence and timing of thrombotic events occurring

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after initial presentation with an acute DVT, as well as the impact of these events on ultimate valve function, in a series of patients monitored prospectively with duplex ultrasonography. For the purpose of this study, such thrombotic events were defined to include rethrombosis of a partially occluded or recanalized venous segment (rethrombosis), propagation of thrombus to uninvolved segments in the ipsilateral limb (propagation), and development of new thrombi in a contralateral uninvolved extremity (new contralateral thrombi).

PATIENTS AND METHODS

Between January 1987 and June 1994, all patients admitted to the University of Washington Medical Center with an acute lower extremity DVT confirmed by venous duplex ultrasonography have been asked to participate in a long-term study of the natural history of DVT. The study protocol was approved by the Human Subjects Committee at the University of Washington, and informed consent was obtained at the time of enrollment.

Patients consenting to participate were asked to return at intervals of 1 day, 7 days, 1 month, and every 3 months for the first year after diagnosis of an acute DVT. Follow-up visits occurred yearly after the first year. At each visit patients were questioned with regard to symptoms, risk factors, and treatment; the lower extremities were examined for sequelae of venous disease; and duplex ultrasonography was performed. Duplex examinations were performed with an Ultramark 8 or 9 scanner (Advanced Technology Laboratories, Bothell, Wash.) with the patient in the 15-degree reverse Trendelenburg position. A 5 MHz transducer was used to obtain an image of the cephalad venous segments, and a 10 MHz transducer was used for the tibial veins. A pulsed-wave Doppler frequency of 5 MHz was used throughout.

To facilitate precise localization of thrombi, the veins of the lower extremity were divided into eight segments including the common femoral vein (CFV) cephalad to the saphenofemoral junction, the deep femoral vein (DFV), the proximal superficial femoral vein (SFP) distal to the saphenofemoral junction, the mid superficial femoral vein (SFM) over the midportion of the thigh, the distal superficial femoral vein (SFD) proximal to the adductor hiatus, the popliteal vein (PPV), the paired posterior tibial veins (PTV), and the greater saphenous vein (GSV) caudal to the saphenofemoral junction. Although imaging of the iliac veins was routinely attempted, they were not included in this analysis because their retroperitoneal location prevents consistent compression and therefore precise classification of these segments. Individual segments were classified as patent, partially occluded, or completely occluded on the basis of duplex criteria. Patent segments were completely compressible with scan head pressure and exhibited spontaneous flow with normal respiratory variation. Spontaneous flow may be normally absent in the posterior tibial veins; these segments were considered patent if they were completely compressible and demonstrated flow with distal augmentation. Partial occlusion was defined as normal or diminished flow in an incompletely compressible segment. An incompressible segment without flow was considered completely occluded. Valvular reflux within a segment was defined as reverse flow persisting for 2 seconds or less with proximal compression or a Valsalva maneuver.

Depending on whether a segment was involved initially, two types of subsequent events could be distinguished by ultrasound criteria. New segmental involvement was considered to have occurred if completely or partially occluding thrombus was identified in a segment that was patent at the initial examination. Rethrombosis of a segment was defined as progression of a partially occluded segment to complete occlusion or of a recanalized segment to either partial or complete occlusion. Because both legs were studied, these ultrasound definitions included three distinct entities—the development of new thrombi in initially uninvolved extremities (new contralateral thrombi); propagation of thrombi to new segments in initially involved limbs (propagation); and rethrombosis of segments thrombosed at presentation (rethrombosis). Newly involved segments (propagation and new contralateral thrombi) were not included in the subsequent analysis of rethrombosis. The time interval to any of these three events was recorded, as well as the ultimate development of reflux within a segment, anticoagulation status, and associated risk factors.

Because most continuous variables were not normally distributed, all results are reported as the median and interquartile range (25th to 75th percentile). All statistical comparisons were made with nonparametric methods by use of the Pearson chi-square with Yates correction or Fischer's exact test for categorical variables and the Mann-Whitney U test for continuous variables. Among extremities, comparisons of thrombus extent between groups were made by use of Kruskal-Wallis one-way analysis of variance with post-hoc comparisons by use of Dunn's test.[7] Contrasts between grouped segments

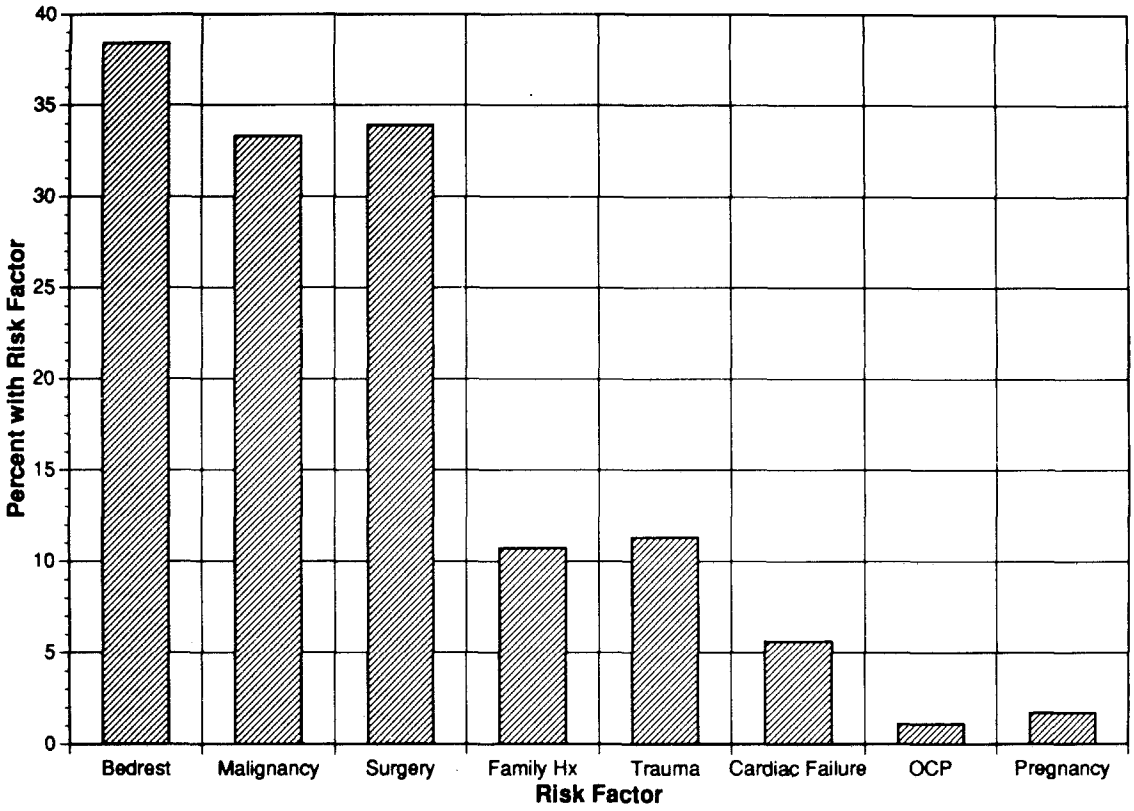

Fig. 1. Risk factors among study patients. Distribution of clinical risk factors for DVT among 177 patients in the study. *OCP* represents oral contraceptives.

within extremities were weighted according to the number of segments in each group and tested with McNemar's test. Comparisons of time to event among the eight individual segments were made by use of Kruskal-Wallis one-way analysis of variance, which assumes independence among the segment categories. Because enrollment in this study has been continuous, follow-up times have differed among patients. In evaluating the development of reflux, the effects of rethrombosis and follow-up duration were evaluated by use of logistic regression. Statistical significance was defined as a p value < 0.05.

RESULTS

Demographics. Since January 1987, 177 patients with DVT of 204 lower extremities have been enrolled in this follow-up study. This group included 98 (55%) men and 79 (45%) women, with a median age of 54.9 (interquartile range 38.5 to 67.3) years. DVT was unilateral on the right side in 56 (32%) patients, on the left side in 94 (53%) patients, and bilateral in 27 (15%) patients. At the time of presentation, a median of 4.0 (3.0 to 6.0) segments per extremity were involved. Median follow-up from the time of enrollment in the study was 9.3 (1.2 to 34.9) months.

In addition to age, clinical risk factors for DVT were considered to include a family history of DVT, concurrent malignancy, pregnancy, use of oral contraceptives, recent surgery, trauma, congestive heart failure, prolonged bed rest, or recent extended (>6 hours) travel. Enrolled patients had a median of 1 risk factor per subject (1.0 to 2.0), with only 29 patients having no risk factors for DVT. The frequency of these risk factors among the study population is illustrated in Fig. 1.

Thrombotic events within extremities. Propagation, rethrombosis, or new contralateral thrombi were identified in 106 extremities in 92 (52%) patients. New thrombi developed in nine previously uninvolved extremities (6%). Among initially involved limbs, propagation alone occurred in 34 extremities, rethrombosis alone in 36 extremities, and both propagation and rethrombosis (in different segments) in 27 extremities. Thus, among initially involved extremities, thrombus propagation oc-

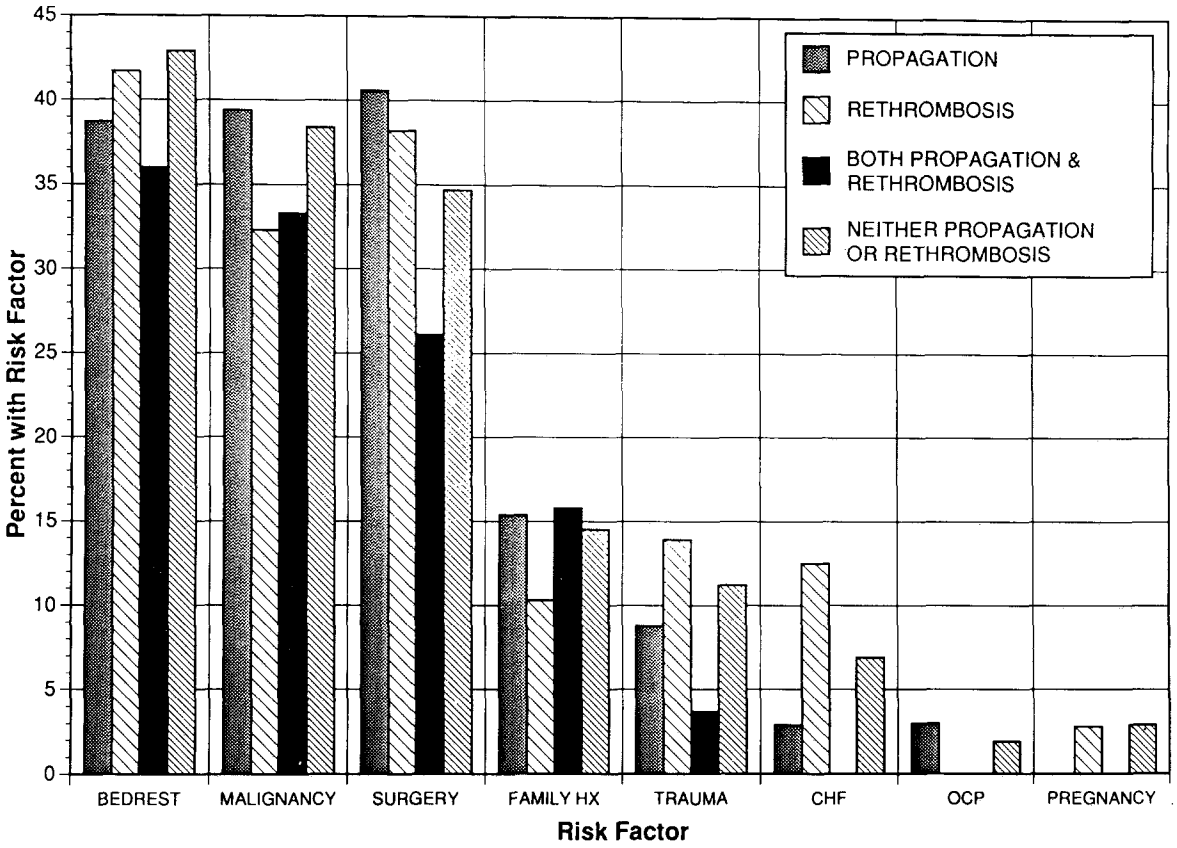

Fig. 2. Risk factors for further thrombotic events. Distribution of clinical risk factors among ipsilateral extremities with thrombus propagation, rethrombosis, both events, or neither event. No statistical difference is present among groups for any risk factor. *CHF* represents congestive heart failure, *OCP* represents oral contraceptives.

curred in a total of 61 (30%) and rethrombosis in 63 (31%) limbs.

Both propagation and rethrombosis were usually limited to a few segments. Among the 61 extremities with propagation to ipsilateral venous segments, thrombus extended to a median of 1.0 (interquartile range 1.0 to 3.0) new segment. Only one or two new segments were involved in 70.5% of extremities. Similarly, rethrombosis affected a median of 1.0 segments (1.0 to 2.0), with only one or two segments involved in 84.2% of such cases. In contrast, new thrombotic events in the contralateral limb involved a median of 4.0 segments (2.0 to 7.0) and involved four or more segments in 55.5% of the extremities.

Among initially involved extremities, further thrombotic events were related to the extent of the initial thrombus. Significant differences in the initial extent of thrombus were present in those extremities with propagation alone, rethrombosis alone, both events, and with neither propagation nor rethrombosis ($p = 0.001$). Propagation tended to occur in extremities with less extensive thrombosis, whereas rethrombosis occurred in those with more extensive thrombosis. A median of 3.0 (interquartile range 2.0 to 4.3) segments were initially involved in limbs with subsequent propagation, in comparison to 5.0 (4.0 to 6.0) segments in extremities with rethrombosis and 4.0 segments in those with either both (3.0 to 5.0) or neither (2.0 to 6.0) event. Post hoc comparison showed the initial extent of involvement to be significantly greater in those with rethrombosis as compared to those with propagation alone ($p < 0.001$) or with neither event ($p < 0.05$). The fewer number of segments involved in those with propagation was not significantly different from those without further events. In contrast to events in the ipsilateral extremity, the development of new thrombi in an initially uninvolved limb was unrelated to the extent of contralateral thrombus.

In comparison to extremities without propaga-

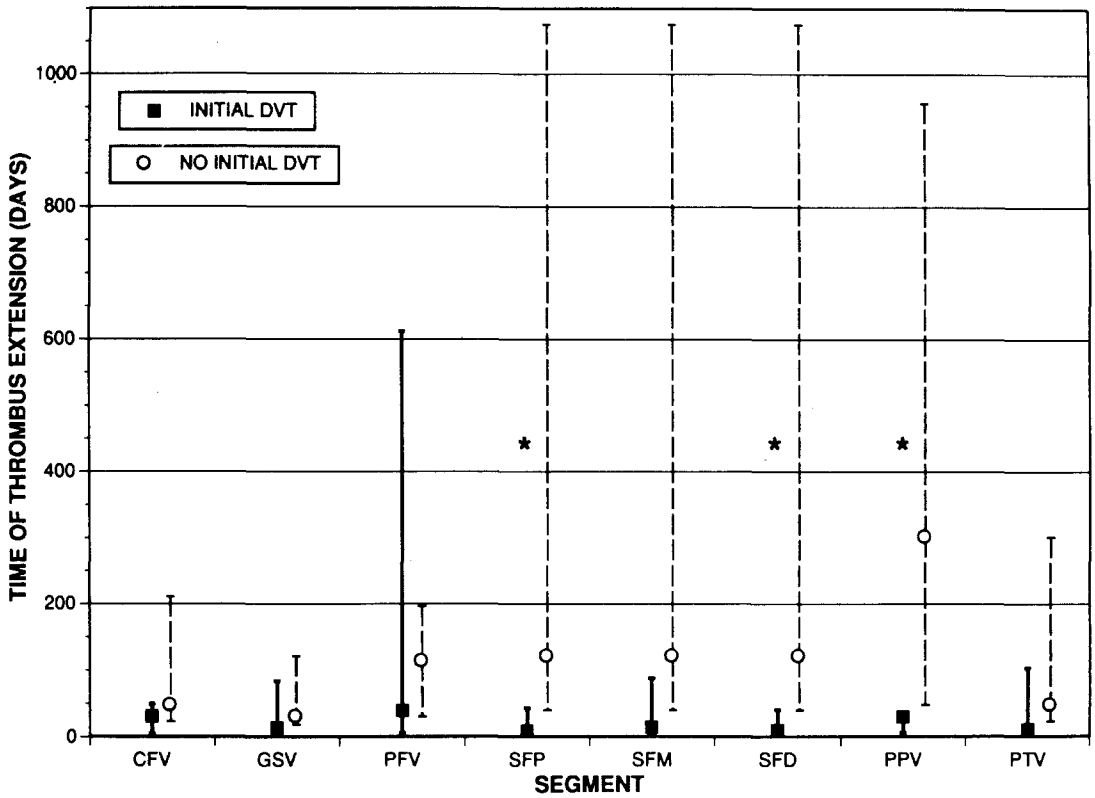

Fig. 3. Median time to new segmental involvement. Time of thrombus extension to uninvolved segments in limbs with (propagation) and without (new contralateral thrombi) DVT at presentation. *Error bars* denote interquartile range (25th to 75th percentile). Differences are statistically significant ($p < 0.03$) for SFP, SFD, and PPV segments.

Table I. Anticoagulation status at the time of subsequent thrombotic events

	Initially involved limb				*Uninvolved limb*	
	Rethrombosis		*Propagation*		*New thrombi*	
Anticoagulation	*No.*	*%*	*No.*	*%*	*No.*	*%*
Heparin	6	9.5	9	14.8	2	22.2
Warfarin	29	46	19	31.1	5	55.6
Both heparin and warfarin	6	9.5	8	13.1	1	11.1
None	18	28.6	21	4.4	1	11.1
Unknown	4	6.3	4	6.6	0	
TOTAL	63		61		9	

tion or rethrombosis, these events were not significantly associated with age, sex, side of involvement, or clinical risk factors including prolonged bed rest, malignancy, surgery, a family history of DVT, heart failure, use of oral contraceptives, pregnancy, recent trauma, or recent prolonged travel (Fig. 2). Similarly, the development of new thrombi in the contralateral extremity was unrelated to any of these factors. Because the treatment of all patients in the study was at the discretion of their primary physician, we have no data regarding the adequacy of anticoagulation in these patients. However, at the time of the subsequent thrombotic event, 88.9% of contralateral extremities with new thrombosis, 59.0% of ipsilateral extremities with propagation and 65.0% of those with rethrombosis were being treated with heparin, warfarin, or both (Table I).

Table II. Thrombotic events among individual venous segments

	Rethrombosis		*Propagation*		*New contralateral DVT*	
Segment	*Segments at risk**	*Rethrombosis*	*Segments at risk†*	*Propagation*	*Segments at risk‡*	*New thrombi*
CFV	291	22 (24.2%)	113	17 (15.0%)	150	5 (3.3%)
GSV	27	2 (7.4%)	177	8 (4.5%)	150	3 (2.0%)
DFV	57	3 (5.3%)	147	10 (6.8%)	150	2 (3.3%)
SFP	109	17 (15.6%)	95	13 (13.7%)	150	5 (3.3%)
SFD	115	20 (17.4%)	89	14 (15.7%)	150	5 (3.3%)
PPV	143	21 (14.7%)	61	9 (14.8%)	150	7 (4.7%)
PTV	146	11 (7.5%)	262	29 (10.3%)	300	9 (3.0%)

*Number of segments initially involved.
†Number of uninvolved segments in ipsilateral extremity.
‡Number of segments in initially uninvolved extremities.

Table III. Median time to propagation and rethrombosis in initially involved extremities

Segment	*No.*	*Propagation time (days)*	*25th to 75th percentile*	*No.*	*Rethrombosis time (days)*	*25th to 75th percentile*	*p Value**
CFV	17	31.0	5.0-49.5	22	62.5	6.0-182.0	0.37
GSV	8	13.5	3.0-83.8	2	61.0	34.0-88.0	0.43
DFV	10	39.5	6.0-612.0	3	7.0	1.0-38.0	0.23
SFP	13	9.0	3.5-43.0	17	41.0	13.0-293.5	0.03
SFM	14	15.0	5.8-88.3	14	61.0	17.8-275.8	0.17
SFD	14	10.0	5.0-41.0	20	232.5	55.8-556.3	0.0005
PPV	9	30.0	6.5-36.5	21	171.0	65.0-376.5	0.002
PTV	29	11.0	3.0-103.5	11	192.0	26.0-224.0	0.02

*Mann-Whitney U test; propagation versus rethrombosis time.

Thrombotic events within segments. The timing of thrombotic events occurring after initial presentation, as well as their effect on ultimate valve function, was addressed within individual venous segments. Among extremities with a DVT at presentation, propagation was observed in 114 of 1037 (11%) initially uninvolved segments. The incidence of propagation (Table II) and the median time to propagation (Table III) were not significantly different among any of the eight segments studied. Propagation tended to be the earliest of the three events examined, occurring within a median of less than 40 days in all segments.

Rethrombosis during follow-up was noted in 110 of 799 (13.8%) initially involved segments. Considering the DFV and GSV as branches of the axial deep venous system, the incidence of rethrombosis was significantly higher ($p < 0.01$) in the axial segments than in the nonaxial GSV and DFV segments (Table II). The time from presentation to rethrombosis was significantly different ($p = 0.03$) among the eight venous segments (Table III). Rethrombosis occurred earlier (7.0 to 62.5 days) in the more cephalad venous segments than in the more caudal SFD, PPV, and PTV segments (171 to 232.5 days). With the exception of the very small number of DFV segments, rethrombosis tended to occur later than propagation in initially involved extremities.

Among uninvolved extremities contralateral to a DVT, new thrombi were observed in 46 of 1037 (3.4%) segments. The incidence of new contralateral thrombi was relatively constant at 2.0% to 4.7% across all segments (Table II). Furthermore, involvement of new segments tended to occur later and with a much broader range in initially uninvolved limbs than in extremities with ipsilateral propagation (Fig. 3). This difference reached statistical significance in SFP, SFD, and PPV segments ($p < 0.03$).

Reflux among segments with and without rethrombosis was compared at the last follow-up visit after excluding those cases in which the reflux status was unknown or indeterminate (Fig. 4). The prevalence of reflux among the cephalad segments (CFV, GSV, and DFV) was not substantially different in those with and without rethrombosis. However, such comparisons are limited by the few numbers of GSV and DFV segments with rethrombosis. In the more caudal segments, reflux developed more commonly in those segments with rethrombosis. This difference in the development of reflux was statistically significant in the SFM, SFD, and PPV segments

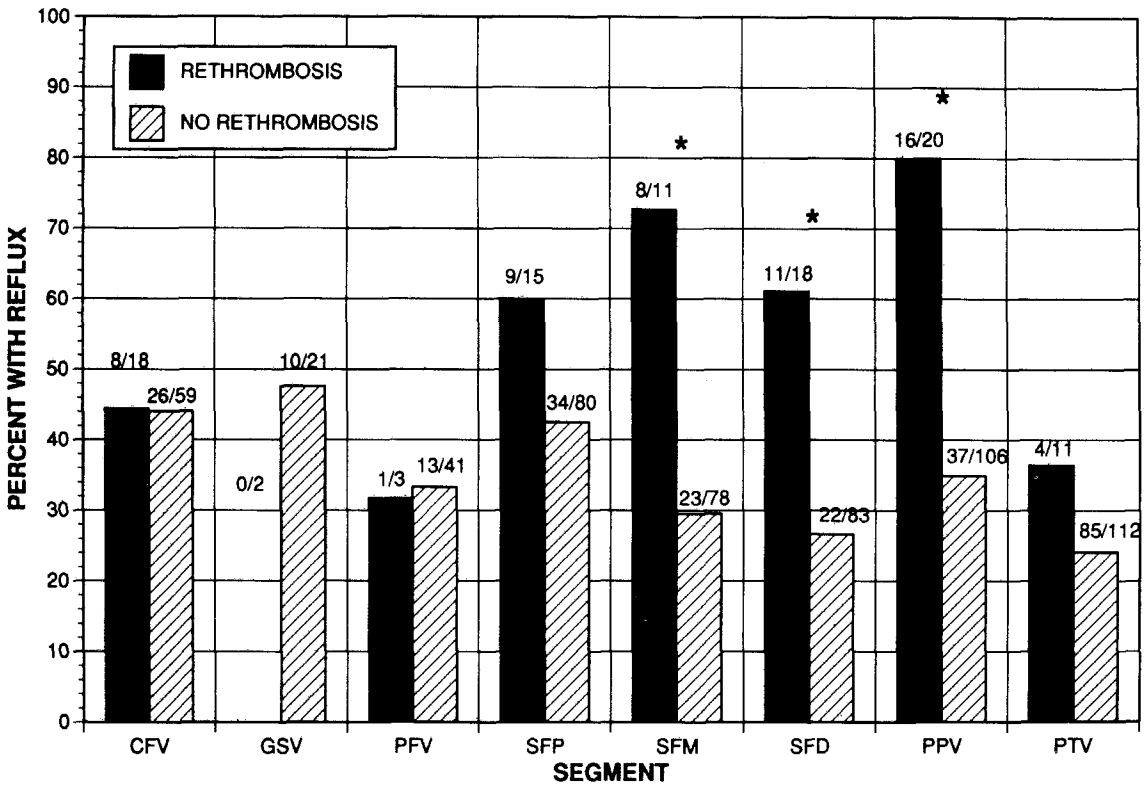

Fig. 4. Reflux in initially involved segments. Reflux status at last follow-up visit among those with and without rethrombosis. *Numbers above bars* indicate number of segments in which reflux was observed over number of segments in which reflux could be definitively assessed. Differences between segments with and without rethrombosis are statistically significant ($p < 0.005$) for SFM, SFD, and PPV segments.

($p < 0.005$). Consistent with the delayed occurrence of rethrombosis, segments with rethrombosis had a longer duration of follow-up than segments without rethrombosis. When those segments with significant differences in the development of reflux were entered into the logistic regression model with duration of follow-up, the occurrence of rethrombosis predicted the development of reflux independent of follow-up interval in the SFM and PPV but not in the SFD segments.

In evaluating segments that thrombosed after initial presentation, the development of reflux was assumed to be dependent only on the presence or absence of thrombus and not on the status of adjacent segments. Segments with propagation and new contralateral thrombi were therefore grouped for analysis. Segments to which thrombus had extended developed reflux in 29% to 50% of cases in comparison to 5.7% to 18.2% of segments that remained patent (Fig. 5). This difference was statistically significant ($p < 0.05$) in all eight venous segments. There was no significant difference in the duration of follow-up among segments that remained patent or developed new thrombus during follow-up.

DISCUSSION

Recanalization of venous thrombi is now recognized as a common phenomenon after an episode of acute DVT.[1-4,8,9] Although the nomenclature remains under debate, the interacting processes of thrombus retraction, peripheral fragmentation, and fibrinolysis lead to restoration of the venous lumen in most cases.[10] However, recurrent thrombotic events are also well recognized. Most clinical investigations have not distinguished propagation from rethrombosis and have tended to include pulmonary embolism with these events. The reported incidence of such events varies with treatment, location of the thrombus, and duration of follow-up. Recurrent thromboembolism has been reported in 0% to 5.2% of patients treated with warfarin for 3 months,[11,12] in 7% of patients monitored for 9 months after a 3-month course of warfarin,[13] and in 47% of patients treated with low-dose subcutaneous heparin for 3

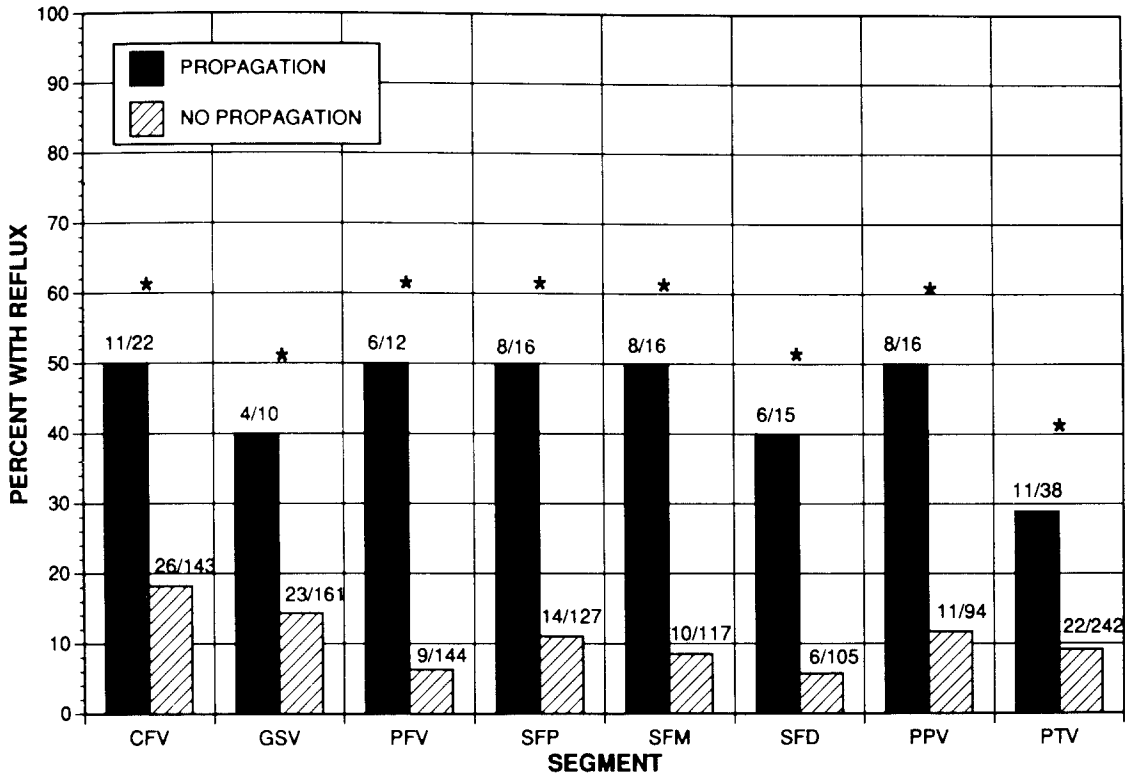

Fig. 5. Reflux in initially uninvolved segments. Reflux status in initially uninvolved segments among those with and without subsequent propagation. *Numbers above bars* indicate number of segments in which reflux was observed over number of segments in which reflux could be definitively assessed. Differences are statistically significant in all eight segments (*asterisk* represents $p < 0.05$).

months after a proximal DVT.[12] On the basis of the literature, Sarasin and Bounameaux[14] calculated a theoretical recurrence rate of 0.9% per month after discontinuing anticoagulant therapy for proximal DVT. Investigations using serial imaging studies have further elucidated the types and frequencies of recurrent thrombotic events. Progression of partially occluding thrombus to complete occlusion has been described in 29% of limbs monitored with phlebography,[15] whereas propagation to a more proximal level has been reported in 38% of patients monitored with serial duplex scanning.[16]

The natural history of acute DVT is therefore perhaps best regarded as a dynamic balance between the competing processes of recanalization and recurrent thrombosis. The occurrence of such conflicting processes should not be surprising given the delicate balance between the coagulation and fibrinolytic systems. In most patients the overall balance appears to favor recanalization early after an acute DVT. However, this balance may be tipped in favor of further thrombosis by factors such as ongoing stimuli to coagulation, hypercoagulable states, and fibrinolytic deficiencies. Such progressive thrombotic events may have important implications for the clinical treament and ultimate outcome of such patients.

As defined in this study, thrombotic events occurring after initial presentation may include extension of thrombus to an initially uninvolved extremity, propagation to new segments in the ipsilateral limb, and rethrombosis of partially occluded or recanalized segments. Whether these events differ in their pathophysiologic mechanism remains unknown, although differences in the timing of their occurrence suggest that they are indeed distinct entities. In this study, propagation to ipsilateral segments tended to occur within a median of less than 40 days. This may suggest persistence of the initial thrombotic stimulus. Indeed, the less extensive initial involvement in limbs with propagation may reflect earlier presentation of these patients. In contrast, development of thrombi in the contralateral limb and rethrombosis tended to occur as somewhat later events. The more extensive segmental involvement of

contralateral extremities further suggests some difference in their pathophysiologic condition.

In this study further thrombotic events occurred in 106 extremities: 97 ipsilateral to the initial thrombus and 9 on the contralateral side. This represents 48% of initially involved and 6% of uninvolved extremities. Among initially involved limbs, propagation and rethrombosis occurred with similar frequency, with both processes occurring together in 13% of extremities. Most importantly, these events appear to be detrimental to valve function. Disregarding the DFV and GSV segments, in which the number of events was quite small, the incidence of reflux among segments with rethrombosis was 36% to 73%. Similarly, initially patent segments to which thrombus had extended demonstrated a 29% to 50% incidence of reflux.

Interpretation of the relationship between rethrombosis and reflux is complicated by the longer follow-up interval among segments with rethrombosis. The duration of follow-up does influence the incidence of reflux, most likely through the progressive occurrence of events such as recanalization and rethrombosis. These longer follow-up intervals among segments with rethrombosis most likely reflect the observation that rethrombosis tends to occur some months after the initial event. Follow-up intervals among those segments with and without propagation, an earlier event, were not significantly different. When the interaction between follow-up interval and rethrombosis was examined by use of logistic regression, rethrombosis remained an independent predictor of reflux in two of the three segments with significant differences in the univariate analysis.

We have previously demonstrated early, complete recanalization after an episode of acute DVT to be an important determinant of ultimate valve function in all segments except the posterior tibial vein.[2] Depending on the venous segment, those segments eventually developing reflux required 2.3 to 7.3 times longer for complete lysis in comparison to those segments in which valve function was preserved. However, a small number of patients were also noted to have development of reflux despite early lysis. It is possible that subsequent thrombotic events are responsible for the development of reflux in at least some of these patients. Such events may also have implications for patients treated with thrombolytic therapy and indeed rethrombosis rates of 60% after treatment with streptokinase have been reported.[17]

Some understanding of the causes of these events and their prevention is essential in minimizing development of the postthrombotic syndrome. Anatomically, rethrombosis occurred in limbs with significantly more extensive segmental involvement, whereas propagation tended to occur in extremities with less extensive initial involvement. Systemic hypercoagulability or fibrinolytic deficiencies may play an important role in uninvolved extremities developing DVT. However, the observation that thrombosis of initially patent venous segments is significantly more common in initially involved compared with uninvolved extremities suggests that local hemodynamic or morphologic factors play at least an important permissive, if not primary, role in these cases. None of the three thrombotic events examined in this study were significantly associated with the clinical risk factors of age, prolonged bed rest, recent surgery, malignancy, a family history of DVT, trauma, congestive heart failure, recent extended travel, use of oral contraceptives, or pregnancy.

This study only partially addresses the causes of further thrombotic events after an episode of acute DVT. Unfortunately, because of this study's design and referral patterns, the relationship of anticoagulation to propagation and rethrombosis cannot be directly addressed. However, it does seem clear that anticoagulation as practiced in the community incompletely prevents these events. At the time of their occurrence, 59.0% to 88.9% of patients were receiving anticoagulants. This clearly does not imply these patients were given therapeutic anticoagulants at the time of the event. Inadequate anticoagulation under therapy has been documented in up to 37% of patients.[16] Although the adequacy of anticoagulation was unrelated to thrombus propagation in the study of Krupski et al.,[16] a much larger study[11] reported the incidence of recurrent venous thromboembolism to be 15 times higher among patients with inadequate anticoagulation for 24 hours or more after starting therapy.

Furthermore, this study does not address the relationship of systemic coagulation and fibrinolytic abnormalities to recurrent thrombotic events. Juhan-Vague et al.[18] reported deficient release of tissue-type plasminogen activator in 10% of patients with DVT; a finding associated with an increased frequency of recurrent thrombotic events. A relationship between impaired fibrinolysis and recurrent DVT has been suggested by several other investigators,[19,20] although the methodologic validity of these findings has been questioned by others.[21] Deficiencies of the coagulation inhibitors antithrombin III, protein C, and protein S are known to be associated with venous

thrombosis, although the prevalence of these deficiencies among patients with DVT is less than 10%.[22] However, resistance to activated protein C has been recently described and appears to be at least 10 times more common among patients with DVT than other heritable anticoagulant deficiencies.[23] Although the relationship of this defect, reported in 33% to 64% of patients with DVT,[23,24] to recurrent DVT remains to be fully defined, it may have important implications for ultimate valve function in these patients.

Despite these gaps in our knowledge, it is becoming clear that venous thrombi undergo a dynamic evolution early after the acute event. Recanalization proceeds rapidly in most patients, although this process is balanced by propagation of thrombus to uninvolved segments as an early event. Extension of thrombus to contralateral uninvolved segments and rethrombosis of involved segments tend to occur somewhat later in all but the most proximal venous segments. Because such events are detrimental to valve competence, identifying patients at risk for these events and preventing their occurrence are of importance in preventing the postthrombotic syndrome. For the present, ensuring an adequate intensity of anticoagulation appears to be important on the basis of the work of Hull et al.,[11] whereas identification of biologic markers of a thrombotic tendency may have some role in the future.

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